Subcutaneous dermatofibrosarcoma protuberans, a rare subtype with predilection for the head: A retrospective series of 18 cases

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Background: Dermatofibrosarcoma protuberans (DFSP) typically affects the dermis and subcutaneous tissue. The subcutaneous variant is rare.

Objective: We sought to characterize the subcutaneous DFSP (SC-DFSP) variant and compare it with cutaneous DFSP (C-DFSP).

Methods: This work was a retrospective study of DFSP treated in our institution.

Results: Of 124 cases of DFSP, 18 were SC-DFSP (14.5%). Except for the deep location, the pathologic and genetic features were indistinguishable from the C-DFSP variant. Histologically, of 18 SC-DFSP cases, 13 were classic DFSP, 3 fibrosarcomatous DFSP (FS-DFSP), 1 Bednar tumor, and 1 giant-cell fibroblastoma. All tumors expressed CD34 and the *COL1A1-PDGFB* fusion transcripts. In our series, higher proportions of SC-DFSP tumors (61%) than C-DFSP tumors (8.5%) were located on the head ($P < .001$). Of the 20 DFSP tumors on the head (16.1%), 11 were SC-DFSP and 9 were C-DFSP.
In addition, half the SC-DFSP tumors affected muscle or periosteum, compared with a quarter of the C-DFSP tumors ($P = .009$). SC-DFSP needed a higher number of Mohs stages than did C-DFSP ($P = .009$). Median follow-up time was 63 months, and 2 FS-DFSP tumors recurred (1 SC-DFSP, 1 C-DFSP).

Limitations: Limitations include the retrospective aspect of the study.

Conclusions: Most DFSP tumors involving the head were subcutaneous and required more complex surgery. Dermatologists should be aware of this atypical presentation, especially in lesions involving the head. (J Am Acad Dermatol 2017;77:503-11.)

Key words: CD34; *COL1A1-PDGFB*; deep; dermatofibrosarcoma protuberans; fibrosarcoma; head; modified Mohs; review; subcutaneous; surgery.

Dermatofibrosarcoma protuberans (DFSP) is a rare, infiltrative skin tumor with high rates of local recurrence and a low risk of metastases.

DFSP usually appears as a poorly circumscribed tumor that infiltrates the dermis, spreading into the underlying subcutaneous tissue. The subcutaneous variant (SC-DFSP) presents as a subcutaneous mass or nodule that shows no connection with the dermis. Clinically, SC-DFSP lacks the typical visible presentation of DFSP and can only be diagnosed through biopsy. SC-DFSP, also known as deep DFSP, was first described by Ezinguer and Weiss[1] and later by Diaz-Cascajo et al.[2] To date, approximately 30

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cases of SC-DFSP have been described in the literature. Nevertheless, the true percentage of this subcutaneous variant and the possible differences between SC-DFSP and cutaneous DFSP (C-DFSP) have not yet been studied in a large series.

We reviewed our series of 124 DFSP cases, aiming to identify SC-DFSP cases and characterize them from a clinical, pathological, and genetic perspective, to compare with the C-DFSP variant.

CAPSULE SUMMARY

- We compared clinical and pathologic features of 18 cases of subcutaneous dermatofibrosarcoma protuberans (SC-DFSP) with 106 cases of cutaneous DFSP.
- A greater proportion of SC-DFSP tumors (61%) than cutaneous DFSP tumors (8.5%) were located on the head ($P < .001$) and involved deep structures ($P = .009$).
- SC-DFSP cases may require more complex surgery.

METHODS

We performed a retrospective, observational study of all patients diagnosed with DFSP who received treatment at the Dermatology Department, Fundación Instituto Valenciano de Oncología, between June 1995 and July 2016.

The cases were selected from the hospital's DFSP database. All cases selected were primary tumors. Informed consent from patients was obtained in accordance with the ethical committee procedures of our hospital.

Diagnosis of DFSP was based on criteria described in the literature.[1,3] Hematoxylin and eosin–stained slides (5-15 per case) were reviewed by 2 authors (B.L., O.S). The tumors were histologically categorized as C-DFSP or SC-DFSP. SC-DFSP was defined according to previous descriptions[2,4,5] when the tumor was located predominantly or exclusively in subcutaneous tissue. In all cases, multiple step sections (between 5 and 10) demonstrated minimal or no cutaneous involvement.

Additional pathologic features were considered: invasion of deep underlying layers (infiltration to subcutaneous tissue, fascia/galea aponeurotica, muscle, periosteum, or bone), a mitotic rate per 10 high-power fields (HPF), the presence of fibrosarcomatous (FS) areas (FS-DFSP), and other histologic variants: giant-cell fibroblastoma; pigmented DFSP; myoid, myxoid, atrophic, granular cell, and sclerotic DFSP.[3]

All cases were immunostained for CD34 protein with the use of a commercially available mouse monoclonal IgG_1 antibody CD34 (QBEnd 10) (Dako Cytomation, Copenhagen, Denmark) at a dilution of 1:50 and stained by use of the avidin-biotin-peroxidase technique.[6] Endothelial cells were used as an internal control for the immunostaining, and a senile hemangioma was used as an external control.

Detection of *COL1A1-PDGFB* transcripts was performed in equivocal or CD34-negative cases by means of multiplex reverse transcriptase–polymerase chain reaction (RT-PCR) or fluorescence in situ hybridization (FISH) techniques on paraffin-embedded tissue samples as previously described.[7,8]

The following clinical information was also analyzed: age, sex, location, time between onset of symptoms and diagnosis (years), tumor size (mm), history of previous trauma (yes/no), magnetic resonance imaging, surgical treatment with modified Mohs technique (paraffin-embedded tissue) (MMS),[8] the number of micrographic stages, local recurrence, disease-free interval, distant metastasis, and follow-up (months).

For the statistical analysis, we used binary variables that reflected the positivity status of the measures of SC-DFSP (yes/no). Associations between the clinicopathologic and SC-DFSP, all categoric, were assessed by use of a χ^2 test to determine homogeneity or linear trend for ordinal variables. A nonparametric test (Kruskal-Wallis) of median values was used for associations between continuous variables and categoric variables. The significance level was set at 5%. All tests used are included in the SPSS statistical software package version 22.0 (SPSS, Inc, Chicago, IL).

We also performed a systematic review of SC-DFSP in the main scientific databases (PubMed/Medline, Scopus, ISI Web of Knowledge), using the key words subcutaneous or deep dermatofibrosarcoma.

RESULTS

Of 182 DFSP cases, 58 were not evaluated for being relapsed cases or because the epidermis, dermis, and subcutaneous tissue were not visible on the same slide. Of 124 primary cases, 18 DFSP cases were subcutaneous (14.5%) (Fig 1). The clinical and pathologic features of the 18 SC-DFSP cases are summarized in Table I and compared with C-DFSP in Table II.

The 18 SC-DFSP cases consisted of 11 women (61%) and 7 men (39%), aged between 14 and 64 years (mean, 39 years). Interestingly, we observed that the most common tumor site was the head (61%) (Fig 2), followed by the trunk (28%) and limbs (11%). The most frequent locations on the head were the